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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,604	09/29/2005	Robert William Holmes	4516-1004	4121

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EXAMINER	
KASSA, TIGABU	

ART UNIT	PAPER NUMBER
1619	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,604	HOLMES ET AL.	
	Examiner	Art Unit	
	TIGABU KASSA	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed September 21, 2009. **Claims 1-11 are currently pending. Claims 1-11 are under consideration in the instant office action.**

Request for continued examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/21/09 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness

Claims 1 and 3-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sorensen et al. (WO 00/74489) in view of Komer (US Patent No. 5773422).

Applicant Claims

Instant claim 1 recites a stable formulation suitable for administration to animals consisting essentially of a combination of levamisole and an avermectin or levamisole and a milbemycin dissolved in a pyrrolidone solvent. Instant claim 3 recites the stable formulation according to claims 1 or 2, wherein the pyrrolidone solvent is 2-pyrrolidone or N-methyl pyrrolidone. Instant claim 4 recites the stable formulation according to claims 1 or 2, wherein the avermectin or milbemycin is present in the range of between 0.01-5% w/v. Instant claim 5 recites the stable formulation according to claim 4, wherein the avermectin or milbemycin is selected from the group consisting of abamectin, doramectin, eprinomectin, ivermectin, and moxidectin. Instant claim 6 recites the stable formulation of according to claims 1 or 2, wherein the levamisole is present in the range of between 1-30% w/v. Instant claim 7 recites a stable formulation suitable for administering to animals consisting essentially of a combination of levamisole and an avermectin or levamisole and a milbemycin dissolved in a pyrrolidone solvent and at least one excipient selected from the group consisting of dietary supplements, vitamins,

mineral, preservatives, stabilizers, flavorants, and co-solvents. Instant claims 8-10 recite the stable formulation suitable for administration to animals as claimed in claims 1 or 2, wherein the formulation is suitable for topical, parenteral, and oral administration, respectively.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Sorensen et al. teach a stable biocidal composition (title) comprising combination of **abamectin 0.20 % w/v**, Tween 80, benzyl alcohol, propylene glycol, Na_2HPO_4, citric acid, **levamisole HCL 8 % w/v**, sodium selenate, and water (page 20, Example 1). Abamectin is dissolved in benzyl alcohol, mixed in Tween 80 and propylene glycol while levamisole is dissolved in Na_2HPO_4, citric acid and sodium selenate. Sorensen et al. teach a combination abamectin/levamisole drench composition comprising **abamectin 0.20 % w/v**, Tween 80, benzyl alcohol, propylene glycol, Na_2HPO_4, citric acid, **levamisole HCL 8 % w/v**, sodium selenate, cellulose gum CMC, and water (page 20-21, Example 2). Sorensen et al. teach a combination abamectin/levamisole drench composition comprising **abamectin 0.20 % w/v**, Tween 80, benzyl alcohol, propylene glycol, Na_2HPO_4, citric acid, **levamisole HCL 8 % w/v**, sodium selenate, carbopol 934, and water (page 21, Example 3). Sorensen et al. also teach a combination abamectin/levamisole drench composition comprising **abamectin 0.20 % w/v**, Tween 80, benzyl alcohol, propylene glycol, Na_2HPO_4, citric acid, **levamisole HCL 8 % w/v**, sodium selenate, xanthan gum, and water (page 21, Example 4).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Sorensen et al. do not explicitly teach the incorporation of the pyrrolidone solvent in the formulation. Although Sorensen et al. teach drench formulations as known by one of ordinary skill in the art can be topically or orally administered, Sorensen et al. are silent whether the form

of administration is topical, parenteral, or oral. These deficiencies are cured by the teachings of Komer.

Komer teaches novel formulations for administration of an avermectin, based on the use of N-methylpyrrolidone or 2-pyrrolidone or mixtures thereof to dissolve the avermectin (see abstract). Komer teaches avermectins are sufficiently soluble in N-methylpyrrolidone or 2-pyrrolidone and mixtures of the two, to permit them to be used as suitable solvents for ivermectin formulations for intramuscular injection, subcutaneous **injection, topical pour-on, stomach intubation, oral and drench administration** (column 2, lines 11-16). Furthermore, Komer teaches illustrative working examples for the different routes of administration, such as injectable, pour-on (topical) formulation, and oral formulations (see column 4, lines 30-67 and all column 5 and column 6, lines 1-31). Komer also teaches formulations including N-methylpyrrolidone, or 2-pyrrolidone and mixtures thereof, **have the advantages of providing higher concentrations of avermectin, allowing smaller dose quantities to be delivered, having improved stability and extended shelf life, increased concentrations of avermectin in the bloodstream and other extracellular fluid compartments and less pain, swelling and tissue damage at the injection site compared to currently available formulations (column 2, lines 47-55)**. N-methylpyrrolidone and 2-pyrrolidone can also be used for transdermal absorption applications such as pour-on formulations and transdermal patches (column 2, lines 55-58). Formulations including N-methylpyrrolidone and/or 2-pyrrolidone can be designed to provide therapeutic levels of avermectin over a sufficient period of time to be more effective against ectoparasites (column 2, lines 58-61).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to an ordinary skilled artisan at the time the instant invention was made to modify the formulation of Sorensen et al. by incorporating the pyrrolidone organic solvent because Komer teaches the use of pyrrolidone solvents N-methylpyrrolidone or 2-pyrrolidone and mixtures of the two in an anthelmintic formulation. One of ordinary skill in the art would have been motivated to incorporate the pyrrolidone solvent in the formulation of Sorensen et al. because formulations including N-methylpyrrolidone, or 2-pyrrolidone and mixtures thereof, **have the advantages of providing higher concentrations of avermectin, allowing smaller dose quantities to be delivered, having improved stability and extended shelf life, increased concentrations of avermectin in the bloodstream and other extracellular fluid compartments and less pain, swelling and tissue damage at the injection site compared to currently available formulations (column 2, lines 47-55).** The instant specification clearly describes that levamisole is soluble in aqueous solution (page 3, line 26), whereas avermectins and milbemycins are insoluble in water (page 3, lines 25-26). Therefore, the solubility problem to be solved is for the avermectin as also clearly taught by Komer that this problem is solved by the use of pyrrolidone solvents N-methylpyrrolidone, or 2-pyrrolidone and mixtures thereof. A skilled artisan would have had a reasonable expectation of success upon combination of the prior art teachings because Sorensen et al. and Komer teach similar compositions for similar purposes namely control of parasitic infections.

It would have been prima facie obvious to an ordinary skilled artisan at the time the instant invention was made to modify the formulation of Sorensen et al. by preparing it for parenteral administration, because Komer teaches formulations containing anthelmintic agents for parenteral administration. One of ordinary skilled artisan would be motivated to have such a

composition for parenteral administration, because it is a conventionally known administration system. A skilled artisan would have had a reasonable expectation of success upon combination of the prior art teachings because Sorensen et al. and Komer teach similar compositions for similar purposes namely control of parasitic infections.

In light of the forgoing discussion, one of ordinary skill in the art would have concluded that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 2 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sorensen et al. (WO 00/74489) in view of Komer (US Patent No. 5773422), Huet et al. (US Patent No 6,426,333), and Harvey (US Patent No 6,165,987).

Applicant Claims

The claimed subject matters of instant claim 1 are set forth above. Instant claim 2 recites a stable formulation suitable for administering to animals consisting essentially of a combination of levamisole and an avermectin or levamisole and a milbemycin dissolved in a pyrrolidone solvent and a co-solvent selected from the group consisting of glycol ethers. Instant claim 11 recites method of treating infection of cattle with Cooperia or Ostertagia by administering a formulation recited in claim 1 or 2.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of the Sorensen et al. and Komer are set forth above.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Sorensen et al. and Komer lacks the teaching of formulations comprising glycol ethers as an additional solvent. This deficiency is cured by the teachings of Huet et al and Harvey. Although Sorensen et al. teach a method of treating a ruminant mammal for nematodes, trematodes and/or cestodes comprising orally administering the formulation taught above, Sorensen et al. and Komer lack the teaching of a method of treating infection of cattle with *Cooperia* or *Ostertagia* by administering a formulation recited in claim 1. This deficiency is cured by the teachings of Harvey.

Huet et al. disclose spot-on formulation for combating parasites comprising an effective amount of a 1-phenylpyrazole derivative; and/or, an effective amount of a macrocyclic lactone or antiparasitic agent; an acceptable liquid carrier vehicle; and optionally, a crystallization inhibitor (column 4, lines 39-67 and column 6, lines 1-30). Huet et al. disclose that "the liquid carrier vehicle comprises a solvent wherein the solvent is selected from the group consisting of, dipropylene glycol n-butyl ether, ethylene glycol monoethyl ether, ethylene glycol monomethyl ether, dipropylene glycol monomethyl ether, diethylene glycol monoethyl ether, which are glycol ethers (column 6, lines 5-20).

Harvey teaches that the anthelmintic agents need to be administered as solutions by dissolving them in solvents such as glycol ethers to be bio-available; because the solid dosage forms are poorly absorbed by the animal (column 1, lines 22-25).

Harvey teaches "a veterinary composition containing an effective amount of praziquantel, an effective amount of at least one macrolide anthelmintic selected from the group comprising the avermectins and the milbemycins, and a suitable organic solvent selected from the group consisting of glycerol formal, ethyl lactate, benzyl alcohol and N-methyl-2-pyrrolidone and the like, wherein the composition is suitable for administration to warm-blooded non-human animal (see abstract). The composition may be a solution or a paste and may be administered to the recipient animal by injection, drench or as an oral paste (see abstract). A method of treating endo- and ectoparasites in non-human animals is also claimed" (see abstract and claim 13). Harvey also teaches that "target parasite species were Haemonchus, Ostertagia, Trichostrongulus, Cooperia, Nematodirus, Oesophagostomum, Chabertis and Monezia expansa" for treatment (column 10, lines 27-30). Ostertagia and Cooperia refer to two parasitic genera and that Harvey's method is suitable in the treatment of species of each genera. A species necessarily anticipates and obviates its corresponding genus.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to an ordinary skilled artisan at the time the instant invention was made to modify the formulation of Sorensen et al. by incorporating additional solvents like glycol ethers as taught by Huet et al., because Harvey teaches that the anthelmintic agents need to be administered as solutions by dissolving them in solvents such as glycol ethers to be bio-available; because the solid dosage forms are poorly absorbed by the animal (column 1, lines 22-25). The Harvey reference is used to demonstrate the general state of the art with regard to the use of solvents such as glycol ethers in anthelmintic formulations. Furthermore, the glycol ethers are commonly known solvents in the art for providing advantages

of improved stability and extended shelf life to the formulations, when compared to solid dosage forms of said anthelmintics administered to animals. A skilled artisan would have had a reasonable expectation of success upon combination of the Sorensen et al., Komer, Huet et al., and Harvey teachings because Sorensen et al., Komer, Huet et al., and Harvey teach within the same field of endeavor and address the same problem, namely the treatment of parasitic infections.

It would have been prima facie obvious to a person of ordinary skill in the art at the time the instant invention was made to modify the method of Sorensen et al., Komer, and Huet et al. via treating parasitic infections caused by the species *Cooperia* or *Ostertagia* as taught by Harvey, because both *Cooperia* or *Ostertagia* are commonly known parasitic species that infect animals that are targeted for treatment by antiparasitic formulations as also demonstrated by Harvey. A skilled artisan would have had a reasonable expectation of success upon combination of the prior art teachings because Sorensen et al., Komer, Huet et al. and Harvey address the same problem, namely the treatment of parasitic infections, which are caused by the parasitic species.

In light of the forgoing discussion, one of ordinary skill in the art would have concluded that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 1 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sorensen et al. (WO 00/74489) in view of Komer (US Patent No. 5773422) and Harvey (US Patent No 6,165,987, IDS reference).

Applicant Claims

Instant claim 11 recites method of treating infection of cattle with Cooperia or Ostertagia by administering a formulation recited in claim 1 or 2.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Sorensen et al. and Komer are set forth above.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Although Sorensen et al. teach a method of treating a ruminant mammal for nematodes, trematodes and/or cestodes comprising orally administering the formulation taught above, Sorensen et al. and Komer lack the teaching of a method of treating infection of cattle with *Cooperia* or *Ostertagia* by administering a formulation recited in claim 1. This deficiency is cured by the teachings of Harvey.

Harvey teaches "a veterinary composition containing an effective amount of praziquantel, an effective amount of at least one macrolide anthelmintic selected from the group comprising the avermectins and the milbemycins, and a suitable organic solvent selected from the group consisting of glycerol formal, ethyl lactate, benzyl alcohol and N-methyl-2-pyrrolidone and the like, wherein the composition is suitable for administration to warm-blooded non-human animals. The composition may be a solution or a paste and may be administered to the recipient animal by injection, drench or as an oral paste. A method of treating endo- and ectoparasites in

non-human animals is also claimed" (see abstract and claim 13). Harvey (US Patent No 6,165,987) also teaches that "target parasite species were Haemonchus, Ostertagia, Trichostrongulus, Cooperia, Nematodirus, Oesophagostomum, Chabertis and Monezia expansa" for treatment (column 10, lines 27-30). Ostertagia and Cooperia refer to two parasitic genera and that Harvey's method is suitable in the treatment of species of each genera. A species necessarily anticipates and obviates it corresponding genus.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to a person of ordinary skill in the art at the time the instant invention was made to modify the method of Sorensen et al. and Komer via treating parasitic infections caused by the species *Cooperia* or *Ostertagia* as taught by Harvey, because both *Cooperia* or *Ostertagia* are commonly known parasitic species that infect animals that are targeted for treatment by antiparasitic formulations as also demonstrated by Harvey. A skilled artisan would have had a reasonable expectation of success upon combination of the prior art teachings because Sorensen et al., Komer and Harvey address the same problem, namely the treatment of parasitic infections, which are caused by the parasitic species.

In light of the forgoing discussion, one of ordinary skill in the art would have concluded that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Claims 1-11 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIGABU KASSA whose telephone number is (571)270-5867. The examiner can normally be reached on 9 am-5 pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tigabu Kassa 9/23/09

/Mina Haghighatian/
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